REMARKS:

In the Office Action dated December 20, 2005, claims 1-23 and 30, in the above-identified U.S. patent application were rejected. Reconsideration of the rejections is respectfully requested in view of the above amendments and the following remarks. Claims 1-31 have been canceled and new claims 32-66 have been added to the application.

The office action indicates that the abstract should be on a separate sheet in the application. An abstract on a separate sheet is attached to this response.

The office action indicates that a sequence listing and sequence identifiers need to be added to the application. An initial sequence listing in paper and computer readable form is attached to this paper and its entry into the application is respectfully requested. The amendments to the specification have been made to add sequence identifiers and to translate Table I into English. No new matter is introduced by means of these amendments.

Claims 1-5 and 21-23 were objected to for the reasons discussed on page 5 of the office action. Claims 1-5 and 21-23 have been canceled and new claims added to the application which do not include the language which was objected to. In view of the cancellation of claims 1-5 and 21-23, applicants request that this objection be withdrawn.

Claims 3-6, 9, 13 and 23 were rejected under 35 USC§112, second paragraph. Claims 3-6, 9, 13 and 23 have been canceled and new claims added to the application which clarify the language found indefinite and which include sequence identifiers. In view of the cancellation of claims 3-6, 9, 13 and 23, applicants request that this objection be withdrawn.

Claims 1-23 and 30 were rejected under 35 USC §112, first paragraph, as lacking an adequate written description. Claims 1-23 and 30 have been canceled and new claims added to the application which specify that the PLK1 is mammalian PLK1, and that the RNA agent is selected from the group consisting of an RNA, an inhibitory peptide and an antibody. Numerous examples of such RNA agents are described on pages 33-78 of the present application. Applicants contend that in view of the numerous examples in the present application, one skilled in the art would reasonably expect any and all RNA, inhibitory peptides and antibodies which reduce or inhibit the activity of polo like kinase I in mammalian cells to work in the present invention. In view of the above amendments and discussion, applicants request that this rejection be withdrawn.

Claims 1 was rejected under 35 USC §102(b) as anticipated by Holtrich. Holtrich does not disclose an RNA, inhibitory peptide or antibody agent which reduces or inhibits the activity of polo like kinase in mammalian cells can be used to inhibit the development or progress of proliferative diseases. Thus, Holtrich does not anticipate the presently claimed invention and applicants request that this rejection be withdrawn.

Claims 1-4, 20-22 and 30 were rejected under 35 USC §102(b) as anticipated by Elez. Elez does not disclose an RNA, inhibitory peptide or antibody agent which reduces or inhibits the activity of polo like kinase in mammalian cells can be used to inhibit the development or progress of proliferative diseases. Thus, Elez does not anticipate the presently claimed invention and applicants request that this rejection be withdrawn.

Claims 6-11, 13, 14, and 16-18 were rejected under 35 USC §103(a) as unpatentable over Holtrich, Elez and Driscoll. Holtrich and Elez do not teach that an RNA, inhibitory peptide or antibody agent which reduces or inhibits the activity of polo like kinase in mammalian cells can be used to inhibit the development or progress of proliferative diseases. Driscoll does not cure the deficiencies in Holtrich and Elez because one skilled in the art would not use Driscoll's repeat gene construct to reduce or inhibit the activity of PLK1. The promoter which is used by Driscoll, in particular the CMV promoter, leads to the transcription of sequences in addition to those needed for the shRNA. Such by products are clearly unwanted and lead to contaminated RNAs. In contrast to Driscoll, in the present invention, the transcription product is the shRNA which leads to siRNA. This contains a sense spacer and an antisense region, wherein the spacer is excised later. Applicants point out that Driscoll discloses a spacer region between 300-1000 nucleotides in length. The longer a spacer is, the more the hairpin structures are distorted and the hybrid is consequently less stable and not as effective. In addition, in the present application a specific promoter can be used, i.e. the family of Pol III promoters, in particular H1 and U6 promoters. Such promoters are advantageous because they do not result in any unspecific by-products. Applicants contend that one skilled in the art would not be motivated to combine Holtrich and Elez with Driscoll, to reduce or inhibit the activity of PLK1 because of the unspecific by products which result from Driscoll's process. In view of the above discussion, applicants request that this rejection be withdrawn.

Claim 12 was rejected under 35 USC §103(a) as unpatentable over Holtrich, Elez, and Driscoll in view of Kennerdell and Martinek. Kennerdell and Martinek are cited for the disclosure of a hairpin loop RNA and an inverted repeat expression construct which has a

67 nt spacer region. Driscoll discloses a spacer region between 300-1000 nucleotides in length. In contrast, the present invention uses spacers of 3-10 nucleotides. The short spacer length used in the present invention is much more specific and leads to a much more stable siRNA. This is due to the fact that the longer a spacer is, the more the hairpin structures are distorted and the less stable the hybrid is. Attached is a paper by Wakiyama et al. which was published recently and which shows that the stem length ("repeat") must be between 19 and 20 base pairs in order to be effective. Loop lengths between 6 and 10 nucleotides are described as very effective. In general, this paper shows that both parameters are very important for the activity of shRNA. Applicants also point out that Driscoll does not suggest that his construct can be used for inhibitory agents for cancer therapy as in the presently claimed invention. Driscoll discloses applications for Alzheimer's disease, Parkinson's disease etc.

In the present application, not only vectors are described but also the manner in which they can be administered to the blood stream, e.g. intraveneously. The present inventors have also shown that after administering to the blood stream, the vector is indeed found in the tumors and that therefore some activity can be expected. The cited prior art does not describe any PLK-related construct but is mostly concerned with lower organisms and applications thereon (Driscoll). Thus, one skilled in the art would not know how to produce such vectors for the application of PLK in cancer therapy. Due to the differences in the methods and constructs, applicants contend that one skilled in the art would not combine Driscoll with Holtrich and Elez. Kennerdell and Martinek describe a construct similar to Driscoll. However, they also use a spacer which is 76 nucleotides long and which therefore

would have the disadvantages mentioned above. In view of the above discussion, applicants contend that claim 12 (new claim 45) would not have been obvious over the cited prior art and request that this rejection be withdrawn.

Claim 15 was rejected under 35 USC §103(a) as unpatentable over Holtrich, Elez, and Driscoll in view of Noonberg. Noonberg was cited only for the disclosure of U6 Pol III driven expression cassettes for delivering oligonucleotides intracellularly. Noonberg does not suggest or disclose a gene construct which can be used to reduce or inhibit the activity of PLK1 and thus does not cure the above discussed deficiencies in Holtrich, Elez, and Driscoll. In view of this, applicants request that this rejection be withdrawn.

Applicants respectfully submit that all of claims 32-64 are now in condition for allowance. If it is believed that the application is not in condition for allowance, it is respectfully requested that the undersigned attorney be contacted at the telephone number below.

In the event this paper is not considered to be timely filed, the Applicant respectfully petitions for an appropriate extension of time. Any fee for such an extension together with any additional fees that may be due with respect to this paper, may be charged to Counsel's Deposit Account No. 02-2135.

Respectfully submitted,

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